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PACKAGING SYSTEMS

A life cycle assessment of injectable drug primary packaging: comparing the traditional process in glass vials with the closed vial technology (polymer vials)

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Abstract
Purpose This study compares environmental impacts of two primary packaging alternatives used for injectable drugs: the traditional method based on glass vials and the method developed by Aseptic Technologies based on polymer vials. A critical review by an external LCA expert was made.
Methods The boundaries of the systems include the packaging production, the product assembly, the filling process, the distribution and the packaging end-of-life by incineration. The study was made in accordance with the international standards ISO 14040 and ISO 14044. Some data were obtained in the scientific literature or by interview with packaging producers. Ecoinvent databases were also used. The LCA study was made using two methodologies: IMPACT 2002+ and ReCiPe. Some sensibility analyses were performed on different points of uncertainty both on method and on systems (polymer vial body and transport conditions).
Results and discussion Results show an environmental gain using a polymer vial over glass. The impact is reduced by 23% for global warming, 25% for primary energy and 32% for respiratory inorganics. For each production step, the environmental impact of both technologies is nearly the same except for the material production, the filling step and the transportation of the finished goods. The production of the polymer vials, made of fuel, leads to a more important environmental impact, especially concerning global warming and primary energy. On the contrary, the two others steps, i.e. filling and transport of the finished goods are more favourable for the polymer vials. This technology allows the elimination of preparation and sterilisation steps which are highly energy consuming and mandatory in the case of the glass vials filling which are supplied unclean and unsterile. The major source of energy consumption comes from water heating, in order to clean the glass vial components. In addition, the filling process, made with a needle through the cork followed by laser re-sealing, is strongly simplified with additional beneficial impact as reduction of energy consumption and pollutants emissions. The transportation step has shown a more positive impact especially when exported over long distance. The sensitivity analyses show that the hypotheses made in both scenarios are rather conservative.
Conclusions The life cycle assessment methodology has been successfully applied to both systems of production, filling, distribution and end-of-life of vials for injectable drugs. For identical disclosers, the polymer vials system has lower environmental impacts than the glass vials system.

Keywords Glass · IMPACT 2002+ · Life cycle assessment · Packaging · Polymer · Vial

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1 Introduction

This study is based on the life cycle assessment of two primary packagings for injectable drugs: the traditional method with glass vials and the alternative method proposed by Aseptic technologies with polymer vials.

Packaging is a field which produces waste and environmental discussions. This field has to be as cheap as possible for the industrial producer but has to show a good reliability especially in the pharmaceutical field. Some life cycle assessment studies of pharmaceutical compounds have already been made (Jiménez-Gonzalez et al. 2004; Kim et al. 2009). Packaging modifications can permit to reduce environmental impact for an identical compound as shown in different life cycle assessment performed on food (Cordella et al. 2008; Humbert et al. 2009). This paper compares two packaging options in a field where products have a high added value but also where environment is not the most important factor affecting the decisions.

This study was made in accordance with the international standards ISO 14040 and ISO 14044 (ISO 2006a, b). The details and the quality of this study were analysed by a critical review and are supposed to be sufficient for a public presentation. The main results are presented in this paper.

Mr. Bernard De Caevel from Research Development and Consulting (RDC) Environment performed the critical review of this study. The critical review and study reports can be obtained by contacting the corresponding author.

2 Methodology

2.1 Goal definition

The goal of this study is to compare the life cycle analysis of pharmaceutical vials packaging in order to show the best way to package them. Two systems are considered: the alternative one using polymer vials and the most traditional one using glass vials. The studied vials have a usual capacity of 1 mL for both systems.

To achieve this comparison, the modelling of both systems has been realized followed by their life cycle assessment. Further steps are the identification of the highest impact and the most damaging step for both systems.

2.2 Scope definition

The first product investigated in this study is the polymer vial presented on Fig. 1. It is the alternative packaging used for injectable drugs. The traditional packaging for injectable drug is the glass vial presented with its components on Fig. 2. This study takes into account all these components and the final packaging of vials.

Polymer vials packaging is a polypropylene box composed of a sheath, a bottom and a lid which can contain 377 vials. This box is packed by six in a double-layer bag which is placed in a polypropylene box closed with a self-adhesive band and an identification label. This packaging is reused for the final transportation of assembled vials.

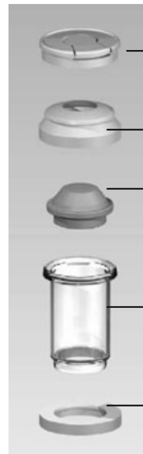

Fig. 1 Polymer vial primary packaging

Glass vials packaging is also a propylene box composed of a sheath and a double bottom which can contain 480 vials. The weight of this box is assessed to be the same with polymer vials packaging. No second box is used in this case.

Final packaging (from the discloser to the client) of both vials is supposed to be the same and is not taken into account in this study.

The packaging systems (for polymer and glass) include stages of vial and components production, sterilisation, transportation, filling, final packaging and incineration. Boundaries of polymer and glass systems are shown respectively on Figs. 3 and 4. All the stages mentioned on Figs. 3 and 4 are taken into account in this study except the utilisation step which is the same for both and neglected in this study.

The functional unit used for further calculation consists of a thousand vials.

2.3 Life cycle inventory analysis

Aseptic Technologies and suppliers provided the majority of data for both systems. Other data come from scientific literature and ecoinvent databases v2.2 (ecoinvent Centre 2010). All material and energy flows are quantified and related to the functional unit. Energy and material quantity using in each steps of the life cycle assessment of packaging vials systems are presented in tables in further paragraphs.

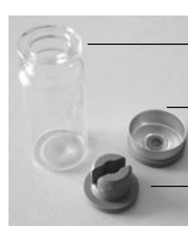

Fig. 2 Glass vial primary packaging

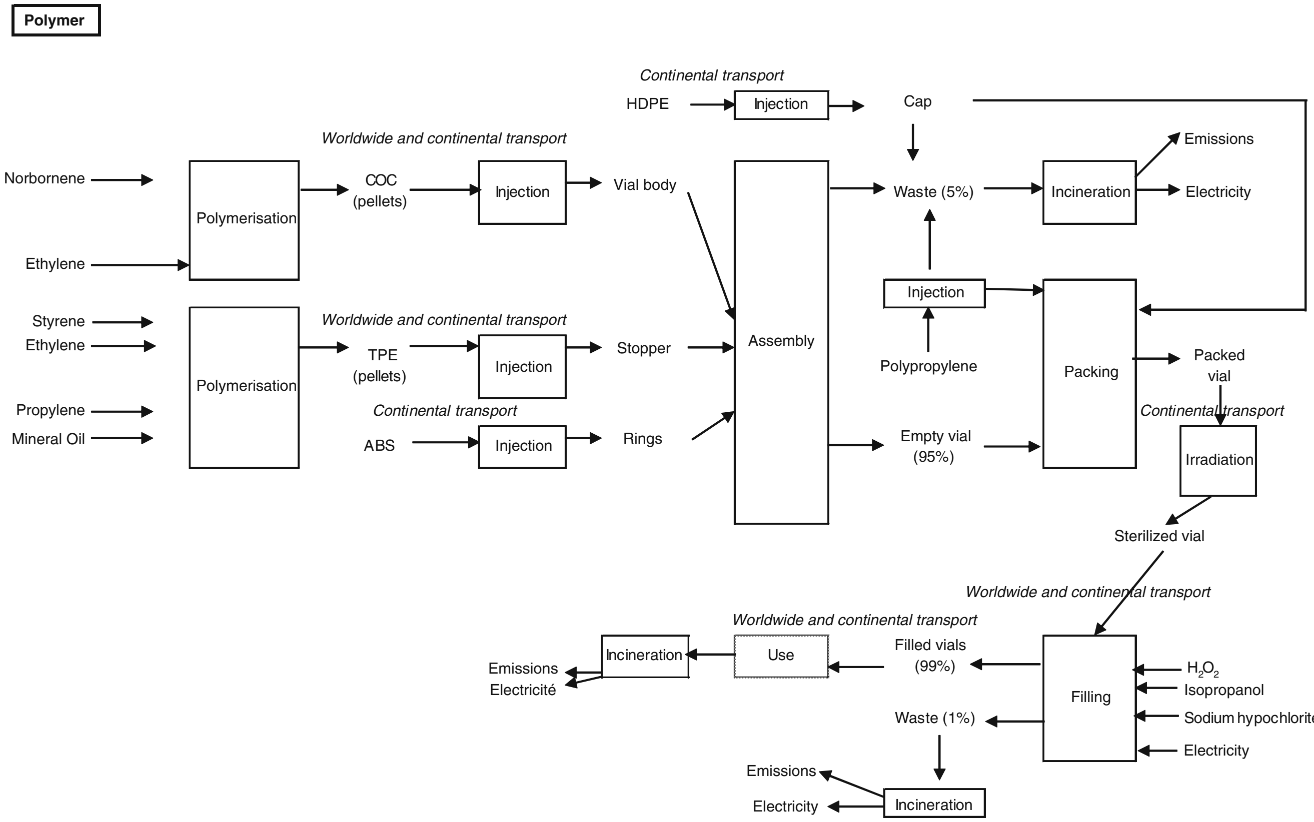

Fig. 3 Polymer system boundaries

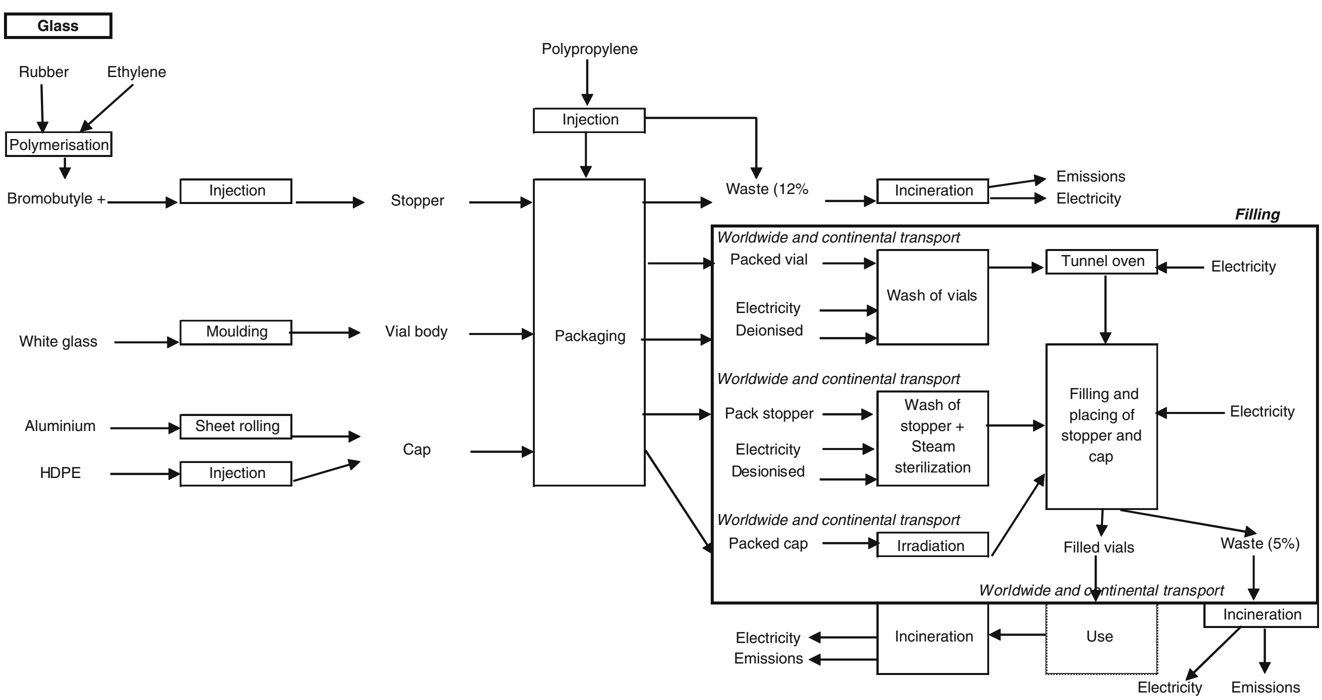

Fig. 4 Glass system boundaries

Table 1 Loss rates of polymer and glass vials systems

Component	Vial manufacturing (%)		Filling (%)	
	Polymer	Glass	Polymer	Glass
Vial body	5	12	1	5
Stopper	5	12	1	5
Cap	5	5	1	5
Rings	5	5	1	5
Packaging	5	5	–	–

2.3.1 Vial manufacturing and packaging

All components presented in Figs. 1 and 2 used for manufacturing of glass or polymer vials are taken into account in the life cycle inventory.

For polymer system, vial body is composed of cyclic olefin copolymer (COC) which is approximately made of 65% of monomer polyethylene units and 35% of monomer norbornene units. Norbornene was approximated by ethylene units. The energy consumption related to the polymer vial material polymerisation was estimated from data given by the producer. Sensitivity analysis on polymer nature was performed in Section 3.3.2.

Glass vial body is made of white glass and is shaped using natural gas and oxygen. These consumptions were given by the glass vial producers.

In the vial manufacturing step, a material loss appears for the starting material (different parts of the bottle and the packaging) by improper handling, breakage or formatting that is not compliant. During the filling step, another loss of material can appear due to breakage or quality controls. The used loss rates are presented in Table 1.

Global energy and material quantity necessary for this step (manufacturing and packaging) are presented in Table 2 for polymer vials system and in Table 3 for glass vials system, using for both the global loss rates showed in Table 1.

Table 2 Reference flows for manufacturing and packaging step for polymer vials system (for the functional unit)

Component	Material	Amount	Unit
Vial body	Ethylene	0.48	kg
	Norbornene	0.48	
	Energy	16	kWh
Cap	HDPE	0.39	kg
Stopper	Polystyrene	0.15	
	Polyethylene	0.08	
	Polypropylene	0.07	
	Mineral oil	0.25	
Rings	ABS	0.89	
Packaging	Polypropylene	1.08	

Table 3 Reference flows for manufacturing and packaging step for glass vials system (for the functional unit)

Component	Material	Amount	Unit
Vial body	White glass	4.48	kg
	Oxygen	1.27	
	Natural gas	52	MJ
Cap	HDPE	0.24	kg
	Aluminium	0.22	kg
Stopper	Rubber	0.50	kg
	Polyethylene	0.13	kg

After manufacturing of the different components, polymer vial is assembled (except for cap which is added after filling), closed and sent to sterilisation. These vials are no longer opened and are transported sealed as opposed to glass vials which components are transported separately and will be closed after filling.

2.3.2 Vial filling

Vial filling is the step that differentiates most the polymer and glass systems.

For polymer system vials are already sterile and cleaned. Filling is realized with a needle passing through the cork followed by laser re-sealing and capping.

For glass system, the components arrived separated at the filling plant and have to be cleaned and sterilized using steam generated from deionised water before filling. Vial bodies are first washed with deionised water and sent to tunnel oven before being filled with injectable drugs. Then they are closed with vial stopper previously sterilized with steam produced from deionised water and cap is added.

Energy and materials consumed in filling step are presented in Table 4.

Electrical energy used is assumed to correspond to the European mix (International Energy Agency 2007) and is composed of coal (30%), natural gas (20%), hydro-electricity (10%), nuclear energy (30%) and fuel (4%). The sum does not equal 100%. The others sources of

Table 4 Reference flows for filling

Raw materials—energy	Polymer	Glass	Unit
Electricity	2.55	14	kWh
Natural gas	–	191	MJ
Deionised water	–	0.09	m^3
Isopropanol	0.03	–	kg
H_2O_2	1.75E-03	–	
Sodium hypochlorite	0.03	–	

Table 5 Distances transportation for polymer system

Polymer				
Component	Market	Percentage of production	Transport	Distance (km)
Raw materials for vial body	Continental	50	Truck	400
	Worldwide	50	Ship	8,000
			Truck	800
Raw materials for stopper	Continental	50	Truck	400
	Worldwide	50	Ship	8,000
			Truck	800
Raw materials for rings	Continental	100	Truck	400
Raw materials for cap	Continental	100	Truck	400
Empty vials to sterilisation	Continental	100	Truck	250
Empty vials to filing	Continental	80	Truck	400
	Worldwide	20	Ship	8,000
			Truck	800
Filled vials to users	Continental	50	Truck	400
	Worldwide	50	Plane	8,000
			Truck	800

electricity such as biomass or tide are supposed to provide no environmental impact.

2.3.3 Transport

Vials are transported by truck, ship or plane. Truck of 28 tons is employed for products transportation, filled or not, on the continental market. Transoceanic ship is used for the empty vials distribution in opposition to intercontinental plane which is used for the filled vials transportation in the worldwide market.

The transport of raw materials for components of glass vial is supposed to be on a local market and is not taken into account in the transport step.

Distribution distances based on the average market for polymer and glass systems can be found in the Tables 5 and 6, respectively. Distances for glass systems are based on actual data and for polymer systems on assumptions on the future place of industry and supposing the same users as glass vials.

Transport of packaging and waste is supposed to be the same for both scenarios and is neglected in this study.

2.3.4 End-of-life

Being pharmaceutical products, all vials, in polymer and in glass, are incinerated. The ecoinvent databases were used for each vial component. The transportation to the

Table 6 Distances transportation for glass system

Glass				
Component	Market	Percentage of production	Transport	Distance (km)
Vial body to filling	Continental	80	Truck	400
	Worldwide	20	Ship	8,000
			Truck	800
Stopper to filling	Continental	50	Truck	400
	Worldwide	50	Ship	8,000
			Truck	800
Cap to sterilisation	Continental	100	Truck	400
Cap to filling	Continental	50	Truck	400
	Worldwide	50	Ship	8,000
			Truck	800
Filled vials to users	Continental	50	Truck	400
	Worldwide	50	Plane	8,000
			Truck	800

Table 7 Inventory of air emissions

Pollutant	Unit	Polymer	Glass
Carbon dioxide (CO_2)	kg	12.47	16.58
Carbon monoxide (CO)	g	18.82	46.82
Dinitrogen monoxide (N_2O)	mg	142.36	228.01
Nitrogen oxides (NO_X)	g	60.66	79.28
Methane (CH_4)	mg	269.29	445.37
Sulphur dioxide (SO_2)	g	3.88	7.20
Particulates, <2.5 μm ($PM_{2,5}$)	g	0.53	1.35
Particulates, >2.5 μm and <10 μm (PM_{10})	mg	95.19	300.17

incinerator was supposed to be the same for both systems and neglected. Incineration emissions were modelled with ecoinvent databases using an incinerator producing electricity, taking into account the average of technologies mix.

Plastic materials produce electricity during their incineration due to the positive lower calorific value. The amount of electricity produced by incineration was calculated and considered as credit for all plastics materials (PE, PP, etc.) for polymer or glass systems. Supplementary energy provided by incineration as heat form is neglected for both systems.

Glass does not burn in an incinerator and does not produce emissions or electricity. Incineration of glass was modelled as the heat necessary to reach 500°C and lost with the cooling of clinker.

2.3.5 Global inventory

Life cycle inventory permits to obtain amount of emitted pollutants for each systems. Some air emissions of main pollutants are presented in Table 7. They are useful to explain results of the life cycle assessment discussed in Section 3.

Table 7 shows lower air pollutants emissions using polymer vials system than glass vials system. Origin of these emissions is explained in Section 3.1.

3 Results and discussion

3.1 Results

Figure 5 shows the impacts of both scenarios for all 15 midpoint indicators of IMPACT 2002+ (Humbert et al. 2009). Water was added to the categories for the characterisation step. It is expressed in cubic meters of water withdrawal.

Table 8 shows impacts results at characterisation step for all midpoints categories. Polymer system obtains for all midpoints categories except carcinogens a more environmental-friendly impact than glass system, especially for mineral extraction which is ten times higher for glass system.

Figure 6 presents normalisation results which permit to identify the most important category in each damage category. Inorganics respiratory is the less environmental-friendly category for human health due to nitrogen and sulphur oxides which are produced during the manufacturing step and the plane transportation. Global warming is the category entirely responsible of the climate change. Carbon dioxide is produced during the vial production step, the plane transportation step and during filling for glass system. Use of non-renewable resources is the most damageable category of the resources damage categories. Vial manufacturing and plane transporta-

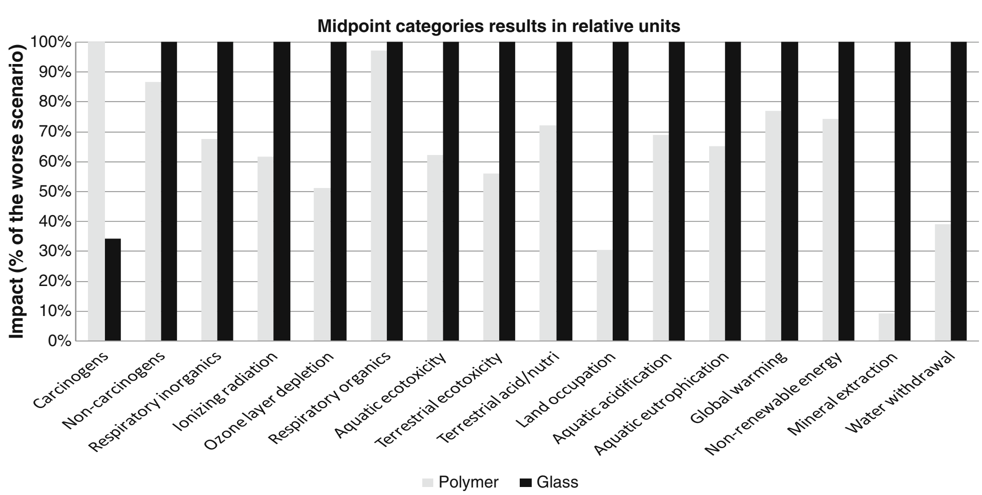

Fig. 5 Comparison of the polymer and the glass vial for all 15 midpoint indicators of IMPACT 2002+

Table 8 Impact results at characterisation step for all midpoint categories

Impact category	Unit	Polymer vials system	Glass vials system
Carcinogens	kg $C_2H_3Cl_{eq}$	2.24E + 00	7.67E-01
Non-carcinogens	kg $C_2H_3Cl_{eq}$	4.41E-01	5.10E-01
Respiratory inorganics	kg $PM_{2.5eq}$	2.53E-02	3.74E-02
Ionizing radiation	BqC-14$_{eq}$	5.85E + 02	9.49E + 02
Ozone layer depletion	kg CFC-11$_{eq}$	4.26E-06	8.32E-06
Respiratory organics	kg C_2H_{4eq}	1.94E-02	1.99E-02
Aquatic ecotoxicity	kg TEG water	1.72E + 03	2.77E + 03
Terrestrial ecotoxicity	kg TEG soil	3.06E + 02	5.47E + 02
Terrestrial acid/nutri	kg SO_{2eq}	7.70E-01	1.07E + 00
Land occupation	m^2org.arable	7.74E-02	2.53E-01
Aquatic acidification	kg SO_{2eq}	1.60E-01	2.33E-01
Aquatic eutrophication	kg PO_4 P-lim	3.93E-03	6.03E-03
Global warming	kg CO_{2eq}	5.05E + 01	6.56E + 01
Non-renewable energy	MJ primary	8.40E + 02	1.13E + 03
Mineral extraction	MJ surplus	6.91E-02	7.52E-01
Water withdrawal	m^3	1.09E-01	2.78E-01

tion are still the most important steps for the environmental damage. Fuel oil is used during the transportation step; natural gas is mostly employed for the vial manufacturing and the filling stage for the glass vial. For ecosystem quality only territorial ecotoxicity category presents a visible impact on Fig. 6, but less important than the others explained above.

As mentioned above inorganics respiratory, climate change and non-renewable resources are the three most important categories.

The produced quantity of inorganic pollutants is reduced by 32%, emissions of carbon dioxide decrease by 23% and economy of resources reaches 25% using the polymer system compared with the glass system. These reductions of pollutants or consumptions should be used with caution in recognizing assumptions and uncertainties of the method which are their origin. Sensitivity analyses have been performed to add strength to these results.

3.2 Steps

To facilitate the comprehension of the most important steps of the life cycle assessment only categories visible on Fig. 6 are presented in Fig. 7.

Carcinogen impact comes mostly from the manufacturing step for both systems. For non-carcinogens category incineration is the cause of the impact for polymer system and the transportation by plane is the origin for glass polymer. The difference of the inorganics respiratory impact between glass and polymer is due to the filling step which leads up to a higher impact for glass system. For climate change category,

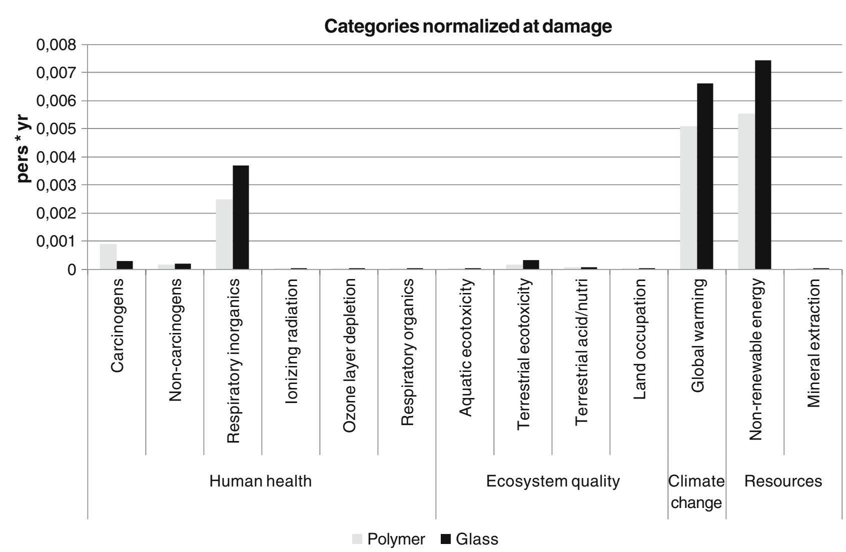

Fig. 6 Comparison of the polymer and the glass vial for 13 categories normalized at damage

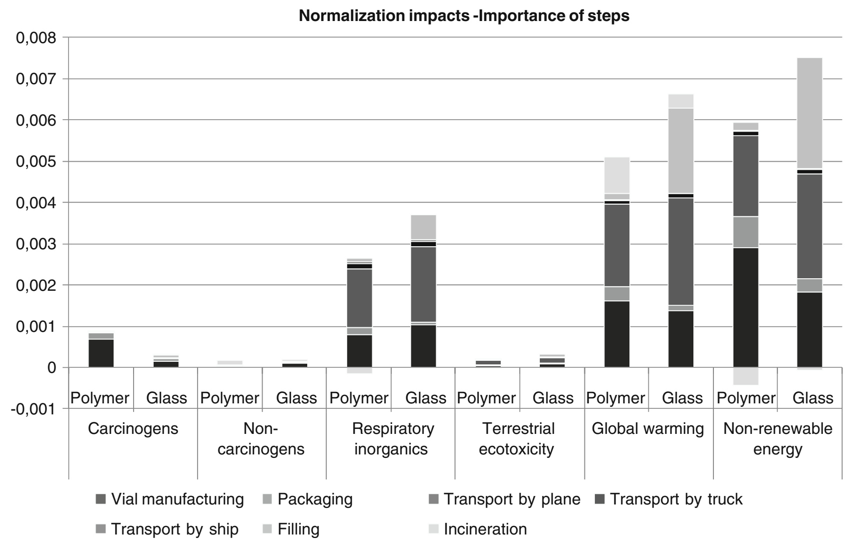

Fig. 7 Comparison of steps importance for polymer and glass systems

incineration step impact is higher in polymer system but filling step and transport by plane reach a more important impact for glass system. For territorial ecotoxicity transportation by plane is the most important step for both systems. For the last category, non-renewable resources, manufacturing, transport by plane and filling are the three significant steps. The first one leads to a bigger impact for polymer system but both others have a superior impact for glass system.

The steps which give the difference between both systems are transport by plane and filling of vials. These two steps permit polymer system to get better results in the three major categories of impact.

3.3 Sensitivity analyses

Many analyses were made to check the hypothesis. The explanations and the results of these analyses are explained in the following paragraphs.

3.3.1 Methodology

The ReCiPe method (Goedkoop et al. 2009) was used with the hierarchist perspective at midpoint. Obtained results are quite similar to those obtained with IMPACT 2002+ method. The ReCiPe method shows a reduction of 31% for inorganic pollutants, 22% for climate change and 25% for non-renewable energy when polymer vials are considered. The main difference between both methods concerns the mineral extraction category (or metal depletion) where extraction reduction reaches 60% for ReCiPe method instead of 90% for IMPACT 2002+.

As mentioned above, percentage of reduction of pollutants can changed with method or assumptions but the trend remains the same, modification of values can come from some uncertainties of used methods.

3.3.2 Change of polymer

Norbornene is a non-usual monomer and had to be modelled by different ways. In the main study, the COC has to be approximated entirely by ethylene and the energy necessary to its production. To value the importance of this factor it should also be modelled using polyethylene and another polymer instead of norbornene as polystyrene or polyethylene terephtalate. The results show a similar impact for all polymers with slightly highest impact for styrene.

3.3.3 Variation of transport

Polymer vial is lighter but also bigger than glass vial (18% bigger). The number of vials in a box is different and higher for glass vial. To take this characteristic into account, truck transport was multiplied by a factor considering the maximum weight possible in truck divided by maximum weight for each scenario. Only transportation between assembling, sterilisation and filling steps is modified according to this factor. Results show a higher impact for each category of both scenarios but polymer vial scenario still gives pollutants reduction compared to glass vial.

Another change for transport is considering only a continental market with a truck transport multiplied by the same previous factor. This is the worst case for polymer vial but it is still the best in each category except for carcinogens.

4 Conclusions and recommendations

The life cycle assessment methodology was successfully applied to two whole systems of production, distribution

and incineration of vials primary packaging, made of polymer or of glass. IMPACT 2002+ method was applied using all 15 midpoint categories and several sensitivity analyses were made changing basic hypotheses or the employed method.

4.1 Conclusions

This study has shown the environmental benefits of the polymer vials thanks to a simplified filling step. The two other important steps are the production of vial and transport by plane which is the least environmental-friendly step. These steps emit in majority inorganic pollutants, carbon dioxide and consume non-renewable resources which belong to the categories with the highest impact for each damage categories (respectively human health, climate change and resources).

4.2 Recommendations

The polymer packaging is interesting via the filling step which is not realisable with glass vials; obtaining a closed and secured glass vial is not feasible at industrial scale. Others steps can also be improved such as transport. Replacing plane by truck or ship when it is possible can also allow the decrease of this impact. The market for the polymer packaging is not well known yet and it could be interesting to adjust the transport distances to make a comparison with the glass market.

Vials packaging is a non-negligible step especially for polymer system where the packaging is composed of two boxes. Another packaging with less weight of plastic could be envisaged to decrease the impact of this step.

This study was performed on vials of 1 mL capacity. A similar study based on products with higher capacity could be interesting to confirm or not the environmental advantage of polymer vials.

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